ANNUAL RESEARCH PROGRESS REPORT

(FY 2010)

GRAND FORKS HUMAN NUTRITION RESEARCH CENTER

UNITED STATES DEPARTMENT OF AGRICULTURE
AGRICULTURAL RESEARCH SERVICE
NORTHERN PLAINS AREA

GRAND FORKS, NORTH DAKOTA 58203

NUTRITIONAL DETERMINANTS OF HEALTH

MANAGEMENT UNIT

5450-010-00

Project Number: 5450-51000-047-00D **Accession:** 0419639 **FY:** 2010

ModeCode: 5450-10-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER
HEALTHY BODY WEIGHT RESEARCH

NPL Leader: DAVID M KLURFELD **Prin Invs:** ERIC O UTHUS

Start Date: 05/24/2010 **Term Date:** 09/30/2014

National Programs: 107 N Human Nutrition

Title: BIOLOGY OF OBESITY PREVENTION

Period Covered **From:** 10 / 2009 **To:** 9 / 2010 **Final Report?** No
Terminate in Two Months? No

Progress and Outcomes:

1a. **Objectives (from AD-416)**

It is not clear whether or how maternal nutrient status during pregnancy epigenetically affects mitochondrial energy metabolism in offspring to increase their susceptibility for developing obesity. Thus, the overall objective is to determine, using animal models, whether low protein intake, high energy intake, or low iron intake during pregnancy influence the development of obesity in offspring through the nutritional programming of mitochondrial function during early development. Specific objectives are: (1) determine whether maternal energy and key nutrient intakes produce epigenetic changes in energy metabolism that contribute to obesity in the offspring, and (2) determine the functional effects of energy, key nutrient intakes and physical activity on obesity-related changes in the expression of genes and protein components of energy metabolism pathways. Within the context of these objectives, the goals of the research are: (1) determine whether protein restriction during pregnancy produces epigenetic changes that, by compromising physiological function, increase the susceptibility of offspring to obesity when fed energy-dense diets; (2) determine whether consumption of diets having excess energy during pregnancy produces long-term mitochondrial dysfunction in offspring that increases their susceptibility to obesity; (3) determine whether low maternal intakes of iron during pregnancy produce mitochondrial dysfunction related to increased susceptibility to obesity in the offspring; and (4) determine whether low maternal intakes of iron during pregnancy impairs mitochondrial adaptation to physical activity in offspring that decreases the effectiveness of physical activity in reducing body weight.

1b. **Approach (from AD-416)**

Three dietary models will be used with laboratory animals. (1) Female rats will be fed diets containing low or normal levels of protein throughout pregnancy. Immediately after birth, the rats fed low protein diets will be changed to normal protein diets. Half of the offspring born to dams fed low protein diet during pregnancy will be weaned to high fat diets and half will be weaned to normal fat diets. Offspring of dams fed normal protein diet during pregnancy will be treated identically. The offspring will remain on the postweaning diets for the remainder of the experiment. (2) Female rats will be fed high or normal fat diets 14 days prior to conception and throughout pregnancy and lactation. Half of the offspring born to dams fed high fat during pregnancy will be weaned to high fat diets and half will be weaned to normal fat diets. Offspring of dams fed normal fat during pregnancy will be treated identically. (3) Female rats will be fed low or normal iron diets 21 days prior to conception and throughout pregnancy and lactation. Half of the offspring born to dams fed low iron during pregnancy will be weaned to high

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fat diets and half will be weaned to normal fat diets. Offspring of dams fed normal iron during pregnancy will be treated identically. In a variation of the low/normal maternal iron model, the offspring will be maintained on either normal or high fat diets for 8 weeks. At the end of 8 weeks, all the offspring will be given normal fat diet and half will be subjected to exercise for 6 weeks. Offspring will be tested for epigenetic changes, changes in glycolytic and oxidative metabolism, muscle and liver mitochondrial function, and mitochondrial oxidative damage over a period of 6 to 36 weeks after being weaned to their postnatal diets. Epigenetic changes will be assessed by determining DNA methylation and the up- and/or down-regulation of differentially methylated genes will be confirmed by real-time PCR. Measurements of mitochondrial function will include respiration, respiratory complex activity and composition, and reactive oxygen production. Oxidative and glycolytic metabolism will be assessed by measuring the activity of key enzymes in the glycolytic and oxidative pathways. Mitochondria are a major source of reactive oxygen species. Assessment of the outcomes of mitochondrial dysfunction will extend to measurement of oxidative and nitrosative damage to mitochondrial proteins and DNA. For metabolic assessment, blood will be analyzed for glucose, triglyceride, insulin, leptin, and adiponectin concentrations. In addition to body weights, adiposity, lean tissue mass, and total body water components of body composition will be assessed by quantitative magnetic resonance.

2. Milestones for FY2010

3. Progress Report

This is the annual report for the new OSQR-approved Project 5450-51000-047-00D that replaces Project 5450-51000-041-00D. (See separate annual report terminating that project.)

One of the goals of the project is to determine whether protein restriction during pregnancy produces epigenetic changes that, by compromising physiological function, increase the susceptibility of offspring to obesity when fed energy-dense diets. An experiment was initiated to accomplish this goal. Female rats were fed either low or normal protein diets for three weeks prior to breeding and throughout pregnancy and lactation. Offspring from these two maternal diet treatment groups were given either normal or high fat diet. The experiment is ongoing and no data has yet been collected from first generation offspring regarding their susceptibility to obesity or epigenetic changes that affect their energy metabolism. Methodology was developed and/or refined for use in the experiment. These methods include DNA methylation arrays, CpG methylation analysis, and PCR methods for mitochondrial gene copy number.

NP / Component Coding

107	3	A	2009
107	4	B	2009

4. Accomplishments

5. Significant Activities that Support Special Target Populations

Project Number: 5450-51000-047-00D Accession: 0419639 FY: 2010

6. Technology Transfer

0 Number of New CRADAs
0 Number of Active CRADAs
0 Number of New MTAs (providing only)
0 Number of Invention Disclosures Submitted
0 Number of Patent Applications Filed
0 Number of New Germplasm Releases
0 Number of new commercial licenses granted
0 Number of web sites managed
0 Number of non-peer reviewed presentations and proceedings
0 Number of newspaper articles and other presentations for non-science audiences
0 Number of Other Technology

7. International Cooperation / Collaboration

Scientific Publications: Log 115

Approved: MCGUIRE MICHAEL R Date: 09/29/2010

Project Number: 5450-51530-010-00D **Accession:** 0415315 **FY:** 2010

ModeCode: 5450-10-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER
HEALTHY BODY WEIGHT RESEARCH

NPL Leader: JOHN W FINLEY **Prin Invs:** LEAH D WHIGHAM GRENDELL

Start Date: 01/26/2009 **Term Date:** 10/31/2011

National Programs: 107 N Human Nutrition

Title: MICRONUTRIENT ROLES IN PHYSIOLOGY AND HEALTH

Period Covered From: 10/2009 **To:** 9 /2010 **Final Report?** No
Terminate in Two Months? No

Progress and Outcomes:

1a. **Objectives (from AD-416)**

Improve health and enhance quality of life by determining, for healthy and at-risk populations (e.g., school-aged children, rural elderly, Native Americans), mineral intakes that promote optimal physiological and psychological development, function and health; develop new functional bases for establishing mineral element requirements; identify mechanisms of action; and determine the influence of sex, age, genetic, lifestyle and environmental factors on mineral element requirements. Develop and implement health promoting interventions for prevention of obesity and co-morbidities in American Indian population in the upper Midwest.

1b. **Approach (from AD-416)**

Dietary intakes and biochemical indices of mineral status will be related to physiologic (e.g., body composition, weight maintenance, physical fitness, energy metabolism, brain and cardiac function) and psychological (e.g., cognition, emotional and social adjustment, school/work performance) measures to determine roles of specific minerals in supporting optimal function and development. A Mobile Nutrition Research Laboratory, Community Studies Unit, and a residential Metabolic Research Unit will be used to conduct epidemiologic, supplementation, fortification, and controlled feeding studies, respectively with healthy and at-risk subjects (e.g., school-aged children, rural elderly, Native Americans). Use qualitative assessment methods (focus groups and in-depth interviews) and surveys to develop and implement social ecological, culturally-sensitive and scientifically sound interventions in American Indian communities. Randomized controlled trials will evaluate the effects of graded intakes of minerals, such as iron, zinc, copper, mangesium and boron, and mediating factors (e.g., genotype, controlled stressors). Animal studies will be used to determine the mechanisms of action of functional outcomes. Studies will involve university, industry and government collaboration.

2. **Milestones for FY2010**

1. Completed phase one of the USDA-ARS multicenter "Healthy Eating and Lifestyle for Total Health" (HEALTH) study.
Milestone Fully Met

3. **Progress Report**

This project is a continuation of Project No: 5450-51000-009-00D and is a bridging research project to the newly proposed project entitled "U.S. Dietary Guidelines Adherence and Healthy Body Weight" that is currently in peer review and expected to be implemented by May 2011.

Project Number: 5450-51530-010-00D Accession: 0415315 FY: 2010

This project identifed barriers/facilitators to adhering to the Dietary Guidelines and determine the effectiveness of dietary and physical activity practices based on the dietary guidelines in preventing unhealthy weight gain and minimizing risk factors for obesity-related chronic disease.

Scientists from ARS and the coordinating Center for the HEALTH study conducted training in nominal group technique methods and completed cognitive interviews of proposed study questions as outlined in the timeline for the HEALTH study. This work was completed in FY2010.

NP / Component Coding

107 2 A 2009

4. Accomplishments

5. Significant Activities that Support Special Target Populations

Scientists in the unit continue to work with American Indians to develop successful partnerships and to promote research on health promotion. This activity includes the continuation of a Cultural Awareness Workshop at United Tribes Community College attended by researchers, technicians, and administrators from throughout the Northern Plains Area. This activity supports Grand Forks Human Nutrition Research Center Programs to improve the nutrition and health of this at-risk and underserved population in the region, and facilitates accomplishment of the objective to promote health and prevent obesity in American Indian communities.

The Specific Cooperative Agreement (Subordinate project #58-5450-6-351 A2) to promote collaborative research partnerships with Cankdeska Cikana Community College (Spirit Lake Reservation) has been continued. This agreement seeks to formalize relationships to initiate discussion geared to develop culturally-appropriate activities and intervention to promote health and prevent obesity and diabetes among American Indians in the Northern Great Plains.

6. Technology Transfer

0 Number of New CRADAs
0 Number of Active CRADAs
1 Number of New MTAs (providing only)
0 Number of Invention Disclosures Submitted
0 Number of Patent Applications Filed
0 Number of New Germplasm Releases
0 Number of new commercial licenses granted
0 Number of web sites managed
0 Number of non-peer reviewed presentations and proceedings
0 Number of newspaper articles and other presentations for non-science audiences
0 Number of Other Technology

New MTA (providing only) Details:

01 MTA ID: 6924
Unique Silicon diet
Description: The diet will be used in research to determine whether th mineral silicon influences the response of mice to a high-fat

Project Number: 5450-51530-010-00D **Accession:** 0415315 **FY:** 2010

(obesogenous) diet.
Transfer: Unique Silicon diet
Customer/User: Medical Research Council
Impact/Outcome: No known impact at this time.

7. International Cooperation / Collaboration

Scientific Publications: **Log 115**

1. Colby, S.E., Johnson, A., Eickhoff, A., Johnson, L. 2009. Promoting Community Health Resources: Preferred Communication Strategies. Journal of Health Promotion Practice. doi:10.1177/1524839909333055. **000022764**
2. Colby, S.E., Johnson, L., Scheett, A., Hoverson, B. 2010. Nutrition Marketing on Food Labels. Journal of Nutrition Education and Behavior. 42(2):92-98. **000020457**
3. Shafer, K.J., Siders, W.A., Johnson, L.K., Lukaski, H.C. 2010. Body Density Estimates from Upper-Body Skinfold Thicknesses Compared to Air-Displacement Plethysmography. Clinical Nutrition. 29(2): 249-254. **000023289**

Approved: MCGUIRE MICHAEL R **Date:** 09/28/2010

Project Number: 5450-51530-010-08S **Accession:** 0411236 **FY:** 2010

ModeCode: 5450-10-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER
HEALTHY BODY WEIGHT RESEARCH

NPL Leader: JOHN W FINLEY **Prin Invs:** GERALD F COMBS

Start Date: 09/19/2006 **Term Date:** 08/31/2011

National Programs: 107 N Human Nutrition

Title: HEALTH PROMOTION IN AMERICAN INDIAN COMMUNITIES

Period Covered From: 10 / 2009 **To:** 9 / 2010 **Final Report?** No
Terminate in Two Months? No

Agreement Number: 58-5450-6-0351

Organization Name: CANKDESKA CIKANA COMM COLLEGE

Progress and Outcomes:

1a. **Objectives (from AD-416)**

The broad objective of this cooperative research is to develop information useful in promoting health through improved nutrition and lifestyles. The specific objectives are to:
1. Develop understanding of the relationships of diet, lifestyle, and the prevalence of chronic diseases, particularly obesity, diabetes, and cardiovascular disease in American Indian peoples;
2. Identify health needs, and the barriers to and facilitators of meeting those needs in American Indian communities;
3. Determine the efficacy of community-based, health-promoting, intervention strategies in American Indian communities; and,
4. Increase research cooperation between American Indian colleges and USDA-ARS.

1b. **Approach (from AD-416)**

Identification and characterization of barriers to and facilitators of eating healthy diets and engaging in healthy lifestyles will be accomplished through a series of focus groups in American Indian communities. Focus groups will be designed to also identify and prioritize community needs as potential mediating factors. Subsequently, health-promoting intervention strategies will be developed and evaluated based on identified barriers and facilitators in the context of community needs and priorities. A research involving human subjects will be conducted with appropriate review and approval by the respective institutional review boards used by Cankdeska Cikana Community College and ARS.

3. **Progress Report**

This report documents research conducted under a Specific Cooperative Agreement between ARS and the CANKDESKA CIKANA COMMUNITY COLLEGE. Additional details for the research can be found in the report for the parent project 5450-51530-010-00D, MICRONUTRIENT ROLES IN PHYSIOLOGY AND HEALTH

Collaborations continued with the Cankdeska Cikana Community College of the Spirit Lake Dakota Nation to continue data analysis of a community needs assessment, and to plan an ancillary study of the multi-center, ARS HEALTH study. Four focus groups were held in FY1010; however none was populated with the target number of participants. Further focus groups will be held in FY2011 to achieve the requisite number.

ADODR monitoring includes site visits, meetings, phone calls, and e-mails.

Project Number: 5450-51530-010-08S **Accession:** 0411236 **FY:** 2010

NP / Component Coding

Approved: MCGUIRE MICHAEL R **Date:** 09/09/2010

Project Number: 5450-51530-010-09N **Accession:** 0412737 **FY:** 2010

ModeCode: 5450-10-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER
HEALTHY BODY WEIGHT RESEARCH

NPL Leader: MARY J KRETSCH **Prin Invs:** GERALD F COMBS

Start Date: 01/01/2008 **Term Date:** 12/31/2012

National Programs: 107 N Human Nutrition

Title: GRAND FORKS COMMUNITY-BASED HEALTH AND FITNESS AGENDA

Period Covered From: 10/2009 **To:** 9 /2010 **Final Report?** No
Terminate in Two Months? No

Agreement Number: 58-5450-8-0101N

Organization Name: GRAND FORKS PARK DISTRICT

Progress and Outcomes:

1a. **Objectives (from AD-416)**

To develop a long-term partnership to foster the development of effective wellness/fitness programs in the Greater Grand Forks Community that will provide opportunities for community based research addressing issues related to the prevention of obesity.

1b. **Approach (from AD-416)**

The Grand Forks Parks District (GFPD) will work with community groups to develop wellness/fitness programs and facilities in the Greater Grand Forks Community. The Grand Forks Human Nutrition Research Center (GFHNRC) will work with the GFPD to advise on issues related to the health needs of citizens, and the design and implementation of those programs/facilities. Both institutions will work together to identify strategic linkages that will meet the goals of the GFPD and advance the research mission of the GFHNRC.

3. **Progress Report**

This report documents research conducted under a Non Funded Cooperative Agreement between ARS and the GRAND FORKS PARK DISTRICT. Additional details for the research can be found in the report for the parent project 5450-51530-010-00D, MICRONUTRIENT ROLES IN PHYSIOLOGY AND HEALTH

ARS scientists collaborated with the Grand Forks Park District in a summer parks based program for 340 elementary schoolers, in which we used sessions emphasizing personal hygiene and healthy food choices. We found subjects in this age group eager to learn about healthy foods when presented in a hands-on, "build your own healthy snack" modality. We also provided advice regarding healthy eating guidelines for local youth programming, and considerations for facilitating community-based health research in a new community wellness facility. ADODR monitoring is done by e-mail, phone calls, and personal contacts.

NP / Component Coding

Approved: MCGUIRE MICHAEL R **Date:** 09/08/2010

Project Number: 5450-51530-010-10N **Accession:** 0414947 **FY:** 2010

ModeCode: 5450-10-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER
HEALTHY BODY WEIGHT RESEARCH

NPL Leader: MARY J KRETSCH **Prin Invs:** GERALD F COMBS

Start Date: 01/01/2009 **Term Date:** 12/31/2013

National Programs: 107 N Human Nutrition

Title: GREAT PLAINS HEALTH RESEARCH CONSORTIUM

Period Covered **From:** 10/2009 **To:** 9 /2010 **Final Report?** No
Terminate in Two Months? No

Agreement Number: 58-5450-9-0105N

Organization Name: UNIVERSITY NEBRASKA MED CNTR

Progress and Outcomes:

1a. **Objectives (from AD-416)**

The University of Nebraska Medical Center (UNMC) will bring together regional institutions with a common interest in rural and other health disparities to establish the Great Plains Health Research Consortium (GPHRC). The ARS-Grand Forks Human Nutrition Research Center will be one of the regional research institutions in this consortium.

1b. **Approach (from AD-416)**

The Great Plains Health Research Consortium will link those research institutions through scientist-to-scientist interactions facilitated by electronic collaboration technologies, and will seek to foster the development of collaborative research projects through the use of funds leveraging, technology/methodology sharing, and some seed funding.

3. **Progress Report**

This report documents research conducted under a Non Funded Cooperative Agreement between ARS and the UNIVERSITY NEBRASKA MEDICAL CENTER (UNMC). Additional details for the research can be found in the report for the parent project 5450-51530-010-00D, MICRONUTRIENT ROLES IN PHYSIOLOGY AND HEALTH

Three ARS scientists presented seminars and participated in strategic planning for developing the consortium research agenda. The GFHNRC hosted the Director of the Great Plains Health Research Consortium to present a seminar and discuss mutual interests. An ARS scientist developed a collaborative project with a Consortium member at the UNMC which they submitted for external funding.

NP / Component Coding

Approved: MCGUIRE MICHAEL R **Date:** 09/23/2010

MICRONUTRIENT ABSORPTION AND METABOLISM

MANAGEMENT UNIT

5450-020-00

Project Number: 5450-51000-045-00D **Accession:** 0418779 **FY:** 2010

ModeCode: 5450-20-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER
DIETARY PREVENTION OF OBESITY-RELATED RESEARCH

NPL Leader: DAVID M KLURFELD **Prin Invs:** HUAWEI ZENG

Start Date: 03/17/2010 **Term Date:** 09/30/2014

National Programs: 107 N Human Nutrition

Title: DIETARY MODULATION OF OBESITY-RELATED CANCER BY SELENIUM

Period Covered **From:** 10/2009 **To:** 9 /2010 **Final Report?** No
Terminate in Two Months? No

Progress and Outcomes:

1a. Objectives (from AD-416)

Determine the dietary modulation of obesity-related cancer by selenium. Specific objectives include 1) Characterize interactions of energy imbalance and dietary Se status on obesity-promoted carcinogenesis; 2) Elucidate the relationship of body mass index (BMI) and features of Se metabolism in selenoprotein genotypes differing in cancer risk.

1b. Approach (from AD-416)

This project will determine the extent to which Se counteracts the carcinogenic effects of obesity. It will do so by elucidating the effects of Se status on obesity-promoted mechanisms of carcinogenesis, and the relationships of BMI and Se metabolism among individuals of two genotypes known to differ in cancer risk. Two forms of dietary Se will be used:
i) SeMet, the dominant form of Se in foods;
ii) precursors of CH3SeH - CH3SeCys (catabolyzed to CH3SeH in the cell), the methylseleninic acid (MSeA) (reduced to CH3SeH in the cell), and the combination of SeMet + recombinant methionase (produces CH3SeH).
The project utilizes the complementary expertise of the research team in molecular/cell biology and cell signaling (Zeng), experimental tumorigenesis (Yan, Zeng), human Se metabolism (Combs), and chemistry/ biochemistry (Jackson, Combs). The collaborative nature of the project is evident in the CH3SeH metabolism/action theme that connects the two objectives. This research builds on in-depth expertise and existing collaborations to investigate a highly relevant problem hitherto not addressed. The Grand Forks Human Nutrition Research Center provides this team of investigators with an experienced professional infrastructure for the efficient recruitment and management of human subjects and the controlled use of animal and cell models.

2. Milestones for FY2010

3. Progress Report
This is the annual report for the new OSQR-approved Project 5450-51000-045-00D that replaces Project 5450-51000-044-00D. (See separate annual report terminating that project.)

This new project focuses on the prevention of obesity-related cancer. We have centered our work on that focus since the project was approved.

To determine the extent to which Se reduces/counteracts the effects of obesity related

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signaling in colon cancer tumorigenesis, we are examining the effect of physical forms (power, pellet) of animal diets on diet-induced obese mice; development of colon xenograft cancer mouse model; selection of the leptin-sensitive colon cells.

To determine the extent to which moderate physical activity enhances the protective effect of dietary Se on obesity-enhanced secondary tumorigenesis, we completed animal feeding for 2 experiments on voluntary physical activity and secondary tumor development using an i.v. injection model and an s.c. injection model in mice. Our preliminary results showed that voluntary physical activity (an average run of 5 km/d on an in-cage running wheel) resulted in significant decreases in body weight and abdominal fat weight, but it did not affect the secondary tumor yield compared with sedentary mice.

To determine the extent to which Se status is inversely associated with risk factors of obesity, we completed data collection for correlation analysis of Se status and biomarkers of chronic inflammation (preliminary human subject retrospective; Study HS009, GFHNRC). We also finished a human study design and initiated IRB proposal preparation for new human subject cross sectional study.
To determine the extent to which obesity exacerbates the altered Se metabolism in individuals, we finished a study design (housed within cross-sectional study, Hypothesis 2.A) and initiated IRB proposal preparation for new human subject cross sectional study; In addition, we initiated data collection for retrospective analysis of the effect of obesity-associated liver dysfunction on Se distribution in archived animal samples derived from previous obesity studies and human liver cell culture experiments.

NP	Component	Coding	
107	2	A	2009
107	3	A	2009

4. Accomplishments

01 It has been well documented that obesity increases the cancer risk. However, there are very few effective animal cancer models and human bioassays which allow us to study obesity related cancer risk. Recently, we have developed several cancer mouse models (colon and seconday cancer) using transplantable cancer cells. In addition, w have established several new assays to study selenium metabolism in the obese population. These models and human bioassays will allow us to characterize interactions of energy imbalance and dietary Se status on obesity-promoted cancer. The information is useful for policy makers and researchers in identifying effective practices that reduce obesity related cancer risk.

107	2	A	2009
107	3	A	2009

5. Significant Activities that Support Special Target Populations

We found that Se status is inversely associated with risk factors of obesity, and believe that the study on Se status of obese population is urgently needed.

Project Number: 5450-51000-045-00D Accession: 0418779 FY: 2010

6. Technology Transfer

0 Number of New CRADAs
0 Number of Active CRADAs
0 Number of New MTAs (providing only)
0 Number of Invention Disclosures Submitted
0 Number of Patent Applications Filed
0 Number of New Germplasm Releases
0 Number of new commercial licenses granted
0 Number of web sites managed
0 Number of non-peer reviewed presentations and proceedings
0 Number of newspaper articles and other presentations for non-science audiences
0 Number of Other Technology

7. International Cooperation / Collaboration

01 GERMANY

We collaborated with the Institut für Experimentelle Endokrinologie; Berlin, Germany for study cooperation with analysis of inflammation and gender-specific effects of obesity on selenoproteins, via email, occasional phone calls and sample exchange.

02 DENMARK

We collaborated with the University of Copenhagen; Copenhagen, Denmark for study cooperation and analysis of biological samples for small-molecule Se species, via email, occasional phone calls, and sample exchange.

Scientific Publications: Log 115

Approved: MCGUIRE MICHAEL R Date: 09/29/2010

Project Number: 5450-51000-045-01R **Accession:** 0410110 **FY:** 2010

ModeCode: 5450-20-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER
DIETARY PREVENTION OF OBESITY-RELATED RESEARCH

NPL Leader: DAVID M KLURFELD **Prin Invs:** GERALD F COMBS

Start Date: 09/01/2005 **Term Date:** 08/31/2010

National Programs: 107 N Human Nutrition

Title: SELENIUM NUTRITION IN HUMANS: PREDICTING DIETARY SELENIUM NEEDS TO ACHIEVE TARGET BLOOD SELENIUM LEVELS

Period Covered **From:** 10/2009 **To:** 9 /2010 **Final Report?** No
Terminate in Two Months? No

Agreement Number: 60-5450-5-0330

Organization Name: NATIONAL CANCER INSTITUTE, DEPARTMENT OF HEALTH AND HUMAN SERVICES, NATIONAL INSTITUTES OF HEALTH

Progress and Outcomes:

1a. **Objectives (from AD-416)**

Develop algorithm relating increase in stable plasma Se level to that at baseline and level of supplemental Se.

1b. **Approach (from AD-416)**

Conduct a randomized, double-blind, intervention study will be conducted with healthy men (120) and women (120) randomized to 0, 50, 100, or 200 ug Se/day (as L-selenomethionine) administered in daily oral doses. Fasting blood samples and urine samples will be drawn two wks prior to and periodically throughout the 1-yr study. The following measurements will be made: Se, homocysteine, vitamin B12 and folate in plasma; Se and 8a-deoxyquanosine in urine; DNA damage and allelic variants of Se-dependent enzymes in lymphocytes. Results will be used to compute the relationship of final-plateau plasma (9-12 mos.) Se concentration as a function of baseline (0 mos.) Se level, Se dose, metabolic body size and urinary Se, as well as outcomes related to carcinogenesis.

3. **Progress Report**

This report documents research conducted under a Reimbursable Agreement between ARS and the NATIONAL CANCER INSTITUTE, DEPARTMENT OF HEALTH AND HUMAN SERVICES, NATIONAL INSTITUTES OF HEALTH. Additional details for the research can be found in the report for the parent project 5450-51000-045-00D, DIETARY MODULATION OF OBESITY-RELATED CANCER BY SELENIUM

We employed a comprehensive method for assessing selenium status in non-deficient subjects based on the direct determination of total plasma selenium, plasma selenoprotein P, and plasma glutathione peroxidase, and imputation from those measurements of total non-specific plasma selenium. Using this approach we found that the non-specific plasma selenium is the only fraction that increases in selenium-adequate individuals fed increasing amounts of food-selenium. We also found that obese individuals (body mass index >30) had depressed levels of selenoprotein P, suggesting that they may be compromised with respect to their ability to transport selenium to peripheral tissues.

NP / Component Coding

Project Number: 5450-51000-045-01R Accession: 0410110 FY: 2010

Approved: MCGUIRE MICHAEL R Date: 10/05/2010

Project Number: 5450-51000-045-02S **Accession:** 0414720 **FY:** 2010

ModeCode: 5450-20-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER
DIETARY PREVENTION OF OBESITY-RELATED RESEARCH

NPL Leader: DAVID M KLURFELD **Prin Invs:** GERALD F COMBS

Start Date: 09/29/2008 **Term Date:** 09/28/2011

National Programs: 107 N Human Nutrition

Title: FOOD-BASED OBESITY PREVENTION AND HEALTH MAINTENANCE RESEARCH

Period Covered **From:** 10/2009 **To:** 9 /2010 **Final Report?** No
Terminate in Two Months? No

Agreement Number: 58-5450-8-0342

Organization Name: UNIVERSITY OF NORTH DAKOTA

Progress and Outcomes:

1a. **Objectives (from AD-416)**

The objective of this cooperative research is to investigate the role of foods and their components in human health, with particular focus on the prevention of obesity, including the endogenous (biological) and exogenous (psycho-social, environmental) factors that affect the maintenance of healthy body weight and risk to co-morbidities of obesity.

1b. **Approach (from AD-416)**

Conduct studies with human volunteers to elucidate functions of and quantitative needs for nutrients and/or other components of foods and physical activity in the support of healthy body weight and minimization of risk to chronic disease. Includes focus groups, cross-sectional and clinical intervention studies in both residential and non-residential settings involving volunteers recruited from Grand Forks and other communities.

3. **Progress Report**

This report documents research conducted under a Specific Cooperative Agreement between ARS and the UNIVERSITY OF NORTH DAKOTA. Additional details for the research can be found in the report for the parent project 5450-51000-045-00D, DIETARY MODULATION OF OBESITY-RELATED CANCER BY SELENIUM

ADODR monitoring is done via on-site meetings, phone calls, and e-mails.

NP / Component Coding

Approved: MCGUIRE MICHAEL R **Date:** 10/05/2010

Project Number: 5450-51000-045-03N **Accession:** 0412134 **FY:** 2010

ModeCode: 5450-20-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER
DIETARY PREVENTION OF OBESITY-RELATED RESEARCH

NPL Leader: DAVID M KLURFELD **Prin Invs:** LIN YAN

Start Date: 08/01/2007 **Term Date:** 12/31/2011

National Programs: 107 N Human Nutrition

Title: ANTICANCER EFFECTS OF HIGH-SELENIUM SOYBEANS

Period Covered **From:** 10/2009 **To:** 9 /2010 **Final Report?** No
Terminate in Two Months? No

Agreement Number: 58-5450-7-0119N

Organization Name: UNIVERSITY OF NEBRASKA

Progress and Outcomes:

1a. **Objectives (from AD-416)**

To investigate whether high-selenium soybeans have greater anticancer effects that low-selenium soybeans in animal models.

1b. **Approach (from AD-416)**

UNL will be responsible for identifying an appropriate line of soybeans (based on its nutrient contents) and determining the stages of the plant development that are most appropriate for selenium fertilization. UNL will be responsible for planting, fertilizing the plants with selenium, harvesting and providing the beans to GFHNRC.

GFHNRC will be responsible for designing and conducting animal studies. This includes dietary preparation, feeding animals, carcinogen treatment, monitoring the progress, collecting and analyzing data.

GFHNRC and UNL together will interpret data, draw conclusions from the investigation and prepare manuscripts for publication in scientific journals.

3. **Progress Report**

This report documents research conducted under a Non Funded Cooperative Agreement between ARS and the UNIVERSITY OF NEBRASKA. Additional details for the research can be found in the report for the parent project 5450-51000-045-00D, DIETARY MODULATION OF OBESITY-RELATED CANCER BY SELENIUM

The agreement with the Nebraska Soybean Board (the funding agency) was that the provided fund could only be used for processing protein isolates from low- and high-selenium soybeans produced at Agronomy Research Farm at University of Nebraska-Lincoln for the planned research. As soybeans harvested from 2007 and 2008 did not reach the targeted level of selenium for the planned work, we planted a new soy cultivar (U03-120139) for 2009 crop year and foliar-applied sodium selenate at different stages of plant and seed development. At the harvest, selenium concentration was 2.5 mg/kg and 0.3 mg/kg for raw seeds from selenium-treated and untreated soy plants. Same as previous years' work, the selenium concentration of the high-selenium soybeans did not reach the targeted level for the planned cancer prevention research. However, it was similar to that of soybeans produced from Northern Plains high-selenium soils. As the funding agency was not able to further extend the funding period, we processed protein isolates using these beans at Food Protein R&D Center, Texas A&M University. These

Project Number: 5450-51000-045-03N **Accession:** 0412134 **FY:** 2010

isolates will be used as a source of plant proteins for studies of the new 5-year research project "Dietary Modulation of Obesity-Related Cancer by Selenium".

NP / Component Coding

Approved: MCGUIRE MICHAEL R **Date:** 10/04/2010

Project Number: 5450-51000-045-04G **Accession:** 0418389 **FY:** 2010

ModeCode: 5450-20-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER
DIETARY PREVENTION OF OBESITY-RELATED RESEARCH

NPL Leader: DAVID M KLURFELD **Prin Invs:** GERALD F COMBS

Start Date: 09/25/2009 **Term Date:** 09/24/2014

National Programs: 107 N Human Nutrition

Title: HUMAN OBESITY PREVENTION RESEARCH

Period Covered **From:** 10 / 2009 **To:** 9 / 2010 **Final Report?** No
Terminate in Two Months? No

Agreement Number: 59-5450-9-0336

Organization Name: UNIVERSITY OF NORTH DAKOTA

Progress and Outcomes:

1a. **Objectives (from AD-416)**

This award will benefit the people of the United States by producing new knowledge that will significantly improve the evidence base for national food, nutrition and health policies. It will bring together two entities, the ARS and the University of North Dakota, each with strong scientific and technical capabilities to produce a combined effort that is unparalleled in its ability to design and conduct human clinical intervention trials addressing the knowledge gaps critical to policy development for reversing the national epidemic of obesity and its co-morbidities. This research will be among the first to test the efficacy and sustainability of U.S. Dietary Guidelines. It will thus be seminal in supporting the further development of those guidelines as well as related national policy concerning food, nutrition and health. Improved national policy will benefit the people of the United States by reducing the prevalence of obesity and obesity-attributable health care costs.

1b. **Approach (from AD-416)**

This research will address the prevention of childhood/adult obesity, which involves food choices/patterns, physical activity and energy balance, metabolism/physiology, genotype/phenotypic expression, food access/composition, attitudes/traditions, and processes that can lead to diabetes, cancer, heart disease and osteoarthritis. This demands innovative, translational research to generate new knowledge and improve the evidence base for national nutrition/health/food policy. This will be accomplished in this project by addressing the following areas:
1. U.S. Dietary Guidelines Adherence and Healthy Body Weight. Research to identify barriers/ facilitators to adhering to the Dietary Guidelines.
2. Biology of Obesity Prevention. Research on metabolism/physiology affected by diet/physical activity in maintaining healthy body weight; use of "omics" tools to understand individuals' responses to interventions and propensities to gain weight.
3. Food Factors in Maintaining Health & Healthy Body Weight. Research examining the effects of food antioxidants on metabolic responses to exercise.
4. Body Weight and Bone Health. Research on the roles of adiposity and body weight on inflammation and bone health.
5. Diet and Physical Activity in Mitigating Obesity-Promoted Carcinogenesis. Research on the effects of adiposity on the metabolism and anticarcinogenic mechanisms of selenium.

Project Number: 5450-51000-045-04G Accession: 0418389 FY: 2010

3. Progress Report

This report documents research conducted under a Grant Agreement between ARS and the UNIVERSITY OF NORTH DAKOTA. Additional details for the research can be found in the report for the parent project 5450-51000-045-00D, DIETARY MODULATION OF OBESITY-RELATED CANCER BY SELENIUM

ARS researchers at the GFHNRC completed a study in which postmenopausal women were supplemented for two years with 600 mg of calcium plus a multi-vitamin containing 400 IU of vitamin D with or without a supplement containing 12 mg of zinc and 2 mg of copper per day. Results showed that the calcium and vitamin supplement slowed bone loss, but that copper and zinc did not enhance that effect in individuals consuming adequate amounts of these minerals according to dietary diaries. Zinc supplementation was beneficial to bone health only in subjects consuming less than the estimated average requirement for zinc.

ARS researchers at the GFHNRC conducted a trial to determine whether consuming meat protein is good or bad for calcium nutrition and bone health. They measured dietary calcium retention in healthy post-menopausal women consuming diets that were low in meat protein and potential acid load or high in meat protein and acid load. A diet rich in protein from meat improved calcium absorption, compensated for increases in urinary calcium, and increased a blood hormone known to stimulate bone formation (insulin-like growth factor I, or IGF-I). These findings indicate that consumption of beef and other meats may be beneficial, rather than detrimental to bone health, and provide evidence useful for developing dietary recommendations for meat protein intake to maintain healthy bones.

To determine the extent to which obesity exacerbates the altered Se metabolism in individuals, we finished a study design and initiated IRB proposal preparation for new human subject cross sectional study. In addition, we initiated data collection for retrospective analysis of the effect of obesity-associated liver dysfunction on Se distribution in archived samples derived from previous obesity studies.

NP / Component Coding

Approved: MCGUIRE MICHAEL R Date: 10/05/2010

Project Number: 5450-51000-046-00D **Accession:** 0419343 **FY:** 2010

ModeCode: 5450-20-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER
DIETARY PREVENTION OF OBESITY-RELATED RESEARCH

NPL Leader: JOHN W FINLEY **Prin Invs:** JAY J CAO

Start Date: 04/09/2010 **Term Date:** 09/30/2014

National Programs: 107 N Human Nutrition

Title: BONE METABOLISM IN OBESITY

Period Covered **From:** 10/2009 **To:** 9 /2010 **Final Report?** No
Terminate in Two Months? No

Progress and Outcomes:

1a. Objectives (from AD-416)

To determine how nutritional, hormonal, and physiological factors affect bone loss/gain in obesity through modifying obesity-induced inflammatory stress. Specifically, we will determine the extent to which obesity is associated with elevated levels of pro-inflammatory cytokines known to promote bone resorption, determine how obesity affects functions of bone cells and bone metabolism, determine the extent to which existing chronic inflammatory stress (induced experimentally by lipopolysaccharide implantation), estrogen deficiency (affected by ovariectomy), and subclinical magnesium intake impair bone health in obese animal models and in obese human subjects, and determine how moderate physical activity preserves bone structure as compared to caloric restriction during weight reduction in an obese animal model.

1b. Approach (from AD-416)

Studies will utilize cell culture, animal models and human subjects. We will use diet-induced obese mice or rats to determine the mechanisms by which adiposity interacts with other dietary, hormonal and physiological factors, such as estrogen deficiency, chronic inflammation, magnesium intake, and moderate exercise, and affects bone structure and functions of osteoblasts and osteoclasts. Human studies will use the in-house Community Studies Unit and the Metabolic Research Unit to conduct supplementation and controlled feeding experiments, respectively. We will determine whether 300 mg/d Mg supplementation to obese postmenopausal women with suspected marginal magnesium deficiency, ameliorates pro-inflammatory cytokine production and improves biomarkers of bone resorption and formation balance.

2. Milestones for FY2010

1. Conduct animal study on obesity on osteoclast activity and bone resorption and finish sample analyses.
   Milestone Fully Met

2. Conduct animal study on estrogen deficiency on inflammatory changes and bone structure and finish sample analyses.
   Milestone Fully Met

3. Conduct experiment determining the effect of marginal Mg deficiency on inflammatory stress of obesity using male rats.
   Milestone Substantially Met

Project Number: 5450-51000-046-00D Accession: 0419343 FY: 2010

. **Progress Report**

This is the annual report for the new OSQR-approved Project 5450-51000-046-00D that replaces Project 5450-51000-039-00D. (See separate annual report terminating that project.)

To determine obesity on osteoclast activity and bone resorption, six-wk-old male C57BL/6mice (n=21) were assigned to two groups and fed either a control (10 kcal% energy as fat) or high-fat diet (HFD, 45 kcal% energy as fat) for 14 weeks. Bone marrow stromal/osteoblastic cells were cultured. Osteoprogenitor activity (alkaline phosphatase positive colonies) and mineralization (calcium nodule formation) were determined. Gene expression was measured using quantitative real-time PCR. Bone structure of proximal and mid-shaft tibia was evaluated by micro-computed tomography. We found that obesity induced by a high-fat diet increases bone resorption and decreases cancellous bone mass but has no effect on cortical bone mass in the tibia in mice. HFD may blunt any positive effects of increased body weight on bone.

To determine whether obesity induced by a high-fat diet exacerbates the increase in inflammatory cytokine production and bone loss caused by estrogen deficiency (ovariectomy), mice with either OVX or sham-operated were be randomly assigned to two groups: one fed a normal-fat control diet, the other a high-fat diet for 3 mos. Changes in bone structure and other serum markers related to bone metabolism were measured.

To determine the effect of marginal Mg deficiency on inflammatory stress of obesity, an experiment was started in March 2010 using male rats; analysis of tissues and fluids from rats fed 50%, 100%, and 150% of the magnesium requirement and either normal or high fat diet for 12 weeks are being analyzed. Rats under similar conditions for 24 weeks will be terminated to obtain tissues and fluids for analysis in October 2010. Only finding to date is that rats fed the high fat diet and 150% the magnesium requirement are the most obese.

NP / Component Coding

107	2	A	2009
107	3	A	2009

4. Accomplishments

01 High-fat diet decreases cancellous bone mass and increases bone resporption in mice: Whether body mass derived from an obesity condition or excessive fat accumulation is beneficial or detrimental to bone has not been established; neither have the mechanisms by which obesity affects bone metabolism. ARS scientists at Grand Forks, ND, demonstrated that mice on a high-fat diet had higher serum tartrate-resistant aci phosphatase and leptin but lower osteocalcin concentrations than those fed the normal fat diet. The high-fat diet increased multinucleated tartrate-resistant acid phosphatase -positive osteoclasts in bone marrow compared to the control diet. Despit being much heavier, mice fed the high-fat diet had lower trabecular bone mass than mice on the control diet. These findings suggest that obesity induced by a high-fat diet increases bone resorption that may blunt any positive effects of increased body weight on bone.

107	2	A	2009
107	3	A	2009

5. Significant Activities that Support Special Target Populations

Project Number: 5450-51000-046-00D Accession: 0419343 FY: 2010

6. Technology Transfer

0 Number of New CRADAs
0 Number of Active CRADAs
0 Number of New MTAs (providing only)
0 Number of Invention Disclosures Submitted
0 Number of Patent Applications Filed
0 Number of New Germplasm Releases
0 Number of new commercial licenses granted
0 Number of web sites managed
0 Number of non-peer reviewed presentations and proceedings
0 Number of newspaper articles and other presentations for non-science audiences
0 Number of Other Technology

7. International Cooperation / Collaboration

Scientific Publications: Log 115

Approved: MCGUIRE MICHAEL R Date: 09/29/2010

Project Number: 5450-51000-048-00D **Accession:** 0419645 **FY:** 2010

ModeCode: 5450-20-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER
DIETARY PREVENTION OF OBESITY-RELATED RESEARCH

NPL Leader: JOHN W FINLEY **Prin Invs:** MATTHEW J PICKLO

Start Date: 05/27/2010 **Term Date:** 09/30/2014

National Programs: 107 N Human Nutrition

Title: FOOD FACTORS AND MAINTENANCE OF BODY WEIGHT AND HEALTH

Period Covered **From:** 10 / 2009 **To:** 9 / 2010 **Final Report?** No
Terminate in Two Months? No

Progress and Outcomes:

1a. Objectives (from AD-416)

1. Determine the extent to which dietary antioxidants alter obesity-induced and/or exercise-induced changes in mitochondrial function and insulin sensitivity.
Sub-objective 1A. Determine the influence of anti-oxidant supplementation on changes in insulin sensitivity induced in the rat by high dietary fat and exercise.
Sub-objective 1B. Determine the degree to which anti-oxidant supplementation alters exercise-induced changes in insulin sensitivity and mitochondrial function responses of overweight/obese individuals.
2. Identify sites and causes of obesity-induced and exercise-induced oxidative stress.
Sub-objective 2A. Determine the effects of obesity and exercise on the temporal and cellular activation of the nuclear factor (erythroid-derived 2)-like 2 (Nrf-2)/Anti-oxidant Response Element pathway.
Sub-objective 2B. Identify and characterize obesity-induced and exercise-induced oxidative changes to insulin signaling pathway proteins.
3. Identify, characterize and compare sites of obesity-induced versus exercise-induced mitochondrial respiratory changes.
Sub-objective 3A. Determine the degree to which anti-oxidant supplementation blunts exercised-induced and obesity-induced changes in mitochondria.

1b. Approach (from AD-416)

In order to complete the objectives of this proposal, we will utilize a combination of studies in humans, rodents that examine physiologic, metabolomic, genetic, and proteomic endpoints. In Objective 1, we will perform studies in humans and rodents to determine how antioxidant (vitamin E and vitamin C) supplementation affects insulin responses to exercise and obesity. The study in humans will involve analysis of exercise adaptation and insulin responses in previously untrained individuals and if antioxidant supplementation either enhances or negates these adaptations. Rodent studies will further examine molecular mechanisms underlying these adaptations.
In Objective 2, we will determine the extent to which obesity, exercise, and anti-oxidant supplementation alter redox balance in animals and specific cells and to identify specific proteins whose thiol redox status is altered in obesity, exercise, and anti-oxidant supplementation. These studies will utilize transgenic mouse models and proteomic approaches.
In Objective 3, we will determine the extent to which obesity, exercise, and anti-oxidant supplementation alter mitochondrial function. These studies will utilize rat models of exercise and obesity. Whole tissue and isolated mitochondria will be studied for changes in total mitochondrial content, mitochondrial gene expression, and respiration, and mitochondrial enzyme activities.

Project Number: 5450-51000-048-00D Accession: 0419645 FY: 2010

2. Milestones for FY2010

3. Progress Report

This is the annual report for the new OSQR-approved Project 5450-51000-048-00D that replaces Project 5450-51000-042-00D. (See separate annual report terminating that project.)

One focus of this project is to determine the extent to which anti-oxidant supplementation alters obesogenic diabetes as well as the positive, insulin-sensitizing and mitochondrial effects of exercise. Another focus is to determine how oxidative stress signaling may be a positive and/or negative response to obesity and exercise depending on the target tissues and proteins. During this time, we have been working on Objective 1 and Objective 2.

For Obj. 1, we have performed initial experiments demonstrating the utility of the obese-prone Sprague-Dawley rat as a model for obesity-induced insulin resistance. Our next step is to induce obesity in these animals in the presence of vitamin E and vitamin C and to determine the extent to which this supplementation prevents insulin resistance. We are also developing the protocol manual for our clinical study evaluating the effects of anti-oxidants upon exercise adaptation in humans. Using tissues from obese versus lean animals we demonstrated that the activity of the oxidant response protein methionine sulfoxide reductase is reduced in the adipose of obese animals and that levels of methionine sulfoxide modified proteins are also reduced. These data are important since methionine sulfoxidation regulates intracellular signaling and thus opens an avenue identifying changes in targets of oxidative stress and how they are altered by obesity. This work will be submitted for publication.

For Obj.2, we are waiting to start the transgenic colony proposed owing to infection of the mice at the provider's facility. We will have to regenerate the line from the infected animals via a third party (e.g. Jackson Labs) that specializes in this procedure. In the mean time, we are pursuing an alternate strategy in which we are using transgenic mice lacking the anti-oxidant response pathway to determine whether they are unable to effectively adapt to exercise. We have begun preliminary proteomic studies to identify sites of oxidative damage to phosphatases (PTEN and PTP1B) involved in insulin signaling.

NP / Component Coding

107	3	A	2009

4. Accomplishments

5. Significant Activities that Support Special Target Populations

Project Number: 5450-51000-048-00D Accession: 0419645 FY: 2010

6. Technology Transfer

0 Number of New CRADAs
0 Number of Active CRADAs
0 Number of New MTAs (providing only)
0 Number of Invention Disclosures Submitted
0 Number of Patent Applications Filed
0 Number of New Germplasm Releases
0 Number of new commercial licenses granted
0 Number of web sites managed
0 Number of non-peer reviewed presentations and proceedings
0 Number of newspaper articles and other presentations for non-science audiences
0 Number of Other Technology

7. International Cooperation / Collaboration

Scientific Publications: Log 115

Approved: MCGUIRE MICHAEL R Date: 09/29/2010

FINAL PROGRESS REPORTS

OF

TERMINATED CRIS WORK UNITS

Project Number: 5450-51000-039-00D **Accession:** 0409965 **FY:** 2010

ModeCode: 5450-10-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER
HEALTHY BODY WEIGHT RESEARCH

NPL Leader: MARY J KRETSCH **Prin Invs:** JAY J CAO

Start Date: 08/01/2005 **Term Date:** 04/08/2010

National Programs: 107 N Human Nutrition

Title: MINERAL INTAKES FOR OPTIMAL BONE DEVELOPMENT AND HEALTH

Period Covered From: 10/2009 **To:** 9 /2010 **Final Report?** Yes
Terminate in Two Months? No

Progress and Outcomes:

1a. Objectives (from AD-416)

Enhance the quality of life through establishing mineral intakes that support optimal bone health. Specifically, determine the amount of dietary calcium needed to maximize calcium retention and minimize bone resorption in postmenopausal women; determine the extent to which dietary protein, specific mineral elements (zinc, copper, magnesium, and boron) and prebiotics (inulin) interact with dietary calcium to affect bone metabolism.

1b. Approach (from AD-416)

Studies will utilize human subjects and animal models. Human studies will use the Mobile Nutrition Research Laboratory, the in-house Community Studies Unit, and the Metabolic Research Unit to conduct epidemiological supplementation, fortification, and controlled feeding experiments, respectively. In each case, subjects will be fed diets containing marginal to high amounts of mineral elements to determine how specific minerals, and interactions among them, affect bone structure (as determined by light microscopy, biomechanical assessment, and densiotometry) and biomarkers [urinary deoxypyridinoline, hemoglobin A1c, and C-reactive protein]). When relevant, the modifying influence of selected hormonal (e.g., estrogen deficiency) or diet compositional (e.g., inulin) factors will be examined.

2. Milestones for FY2010

1. Report whether zinc inhibits osteoclastogenesis through down-regulation of Zip1 transporter.
   Milestone Substantially Met

2. Report growth phase and post growth phase of boron essentiality studies.
   Milestone Substantially Met

3. Progress Report

This is the final report for Project 5450-51000-039-00D, which has been replaced by new OSQR-approved Project 5450-51000-046-00D that is being reported separately.

Requirements for minerals involved in bone metabolism were defined by carefully controlled balance studies with humans. Supplementation trials attested to the importance of nutrients in addition to calcium for bone health, and revealed dietary factors beneficial and detrimental for bone growth and maintenance. Data from 27 controlled human feeding studies indicated that the magnesium requirement for humans should be about 165 milligrams per day. Data from 19 controlled human feeding studies

indicated that calcium requirement should be about 741 milligrams per day.

A study with healthy postmenopausal women showed that a diet high in meat protein was not detrimental to bone health. Although the increase renal acid load induced by the high meat protein intake increased urinary acid excretion, it did not decrease calcium retention or negatively affect bone status indicators. A study in which postmenopausal women were supplemented for two years with 600 milligrams of calcium plus a multi-vitamin containing 400 International Units of vitamin D with or without a supplement containing 12 milligrams of zinc and 2 milligrams of copper per day indicated that the calcium and vitamin supplement slowed bone loss.

The detrimental effect of calcium deficiency on bone structure and strength during adolescence in females can be reversed by subsequent adequate calcium nutriture during early childhood based on studies with rats. Experiments with rats also found that bone mass, structure and biomechanical strength achieved by feeding adequate calcium is not improved by feeding additional calcium; this suggests that increasing dietary calcium intakes beyond those needed to maximize bone density is not an effective method for preventing bone loss leading to osteoporosis.

A study with cell model to determine the function of zinc and zinc transporter, ZIP1, in the osteoclastogenesis process has been conducted. Osteoclast activity and expression of ZIP1 during zinc depletion or supplementation have been measured. Analyses of cell proliferation, apoptosis, osteoclast formation, and gene expression were completed successfully. Zinc deficiency promoted osteoclast activity in RAW cells.

Boron deprivation compared to usual intakes of boron resulted in markedly impaired alveolar bone healing after tooth extraction because of reduced bone formation. Studies with rats suggested that boron is bioactive through modulating the utilization or formation of S-adenosylmethionine involved in numerous biochemical processes, one of which leads to homocysteine. Poor control of homocysteine has been implicated in increased risk for bone fractures and osteoporosis.

Pinto bean hull extract supplementation improved bone structural indices, bone mineral density, and vertebrae trabecular bone thickness in mice. Biochemical changes suggested that bean hull extract may have beneficial effects on bone health by decreasing bone resorption.

NP / Component Coding

107 3 A 2009

4. Accomplishments

01 New estimation of the calcium requirement for men and women. Calcium is an element that may be a risk factor for osteoporosis and current recommendations regarding the amount of calcium needed to support health and optimal biological function are based on sparse balance data. ARS scientists at Grand Forks, ND, established a new estimation of the average calcium requirement of healthy men and women by conducting secondary analyses of calcium balance data generated in 19 human controlled feeding studies at the Grand Forks Human Nutrition Research Center over the last three decades. The findings suggest a calcium requirement for healthy men and women (741 milligrams/day) that is lower than that estimated previously. This work will be very useful in setting the next Dietary Reference Intake for calcium.

107 2 A 2009

02 Adequate zinc is beneficial for bone health in postmenopausal women. Zinc

supplementation is beneficial for bone density in women with dietary intakes less tha the estimated average (EAR) for zinc. Limited studies have suggested that supplemental intakes of copper and zinc attenuate bone loss in post menopausal women. ARS researchers at Grand Forks, ND, supplemented postmenopausal women for two years with 600 milligrams of calcium plus a multi-vitamin containing 400 International Unit of vitamin D with or without a supplement containing 12 milligrams of zinc and 2 milligrams of copper per day. The zinc supplementation slowed the loss of bone mineral density in subjects consuming less than the estimated average requirement for zinc but not in women consuming more than the EAR. This finding indicates that inadequate dietary zinc may be a factor that increases the risk of osteoporosis in postmenopausal women.

107 2 A 2009

03 Inadequate magnesium intake is a risk factor for osteoporosis in postmenopausal women Subclinical (marginal) magnesium deficiency increases the risk for bone loss leading to osteoporosis in postmenopausal women. Very limited human data are available to support the suggestion that magnesium deficiency contributes to the incidence of osteoporosis in postmenopausal women. ARS researchers at Grand Forks, ND, used food diaries to determine that 38% of 224 women in a calcium-copper-zinc supplementation study consumed less than 237 milligrams of magnesium per day, the 95 percentile of th estimated average requirement (EAR) determined by balance data at Grand Forks, ND, bu less than the EAR of 265 milligrams per day set by the US Food and Nutrition Board. These women had a markedly lower mean bone mineral density and t-score (indicator of bone loss) than women consuming more than 237 milligrams per day. These differences suggest that postmenopausal women who regularly consume less than 237 milligrams of magnesium per day have an increased risk for osteoporosis.

107 2 A 2009

04 High meat protein diet with high potential acid load does not impair calcium retention. Whether consuming meat protein is good or bad for calcium nutrition and bone health is controversy. The protein effect on bone is further compounded by a greater renal acid load when emphasizing grain-based foods rather than fruits and vegetables. ARS scientists at Grand Forks, ND, measured dietary calcium retention in healthy post-menopausal women consuming diets that were low in meat protein and potential acid load or high in meat protein and acid load. The diet rich in protein from meat improved calcium absorption that compensated for increases in urinary calcium. The high meat protein diet also increased a blood hormone known to stimulate bone formation (insulin-like growth factor I, or IGF-I). These findings indicate that consumption of beef and other meats may be beneficial, rather than detrimental to bon health. These results provide evidence useful for developing dietary recommendations for meat protein intake to maintain healthy bones.

107 2 A 2009

05 Bone loss induced by calcium deficiency in young rats can be restored by subsequent adequate calcium intake. Achieving maximal bone mass in adolescence is essential to prevent age-related bone loss. Whether inadequate calcium intake before sexual maturity can be corrected by calcium repletion afterwards is not well investigated. ARS scientists at Grand Forks, ND, demonstrated that calcium deficiency caused bone loss in female rats but the loss of bone can be reversed by increasing dietary calciu intake after sexual maturity. The results indicate that adequate calcium intake earl in adulthood is important to increase bone mass and correct low bone mass due to poor calcium nutrition during adolescence. These animal results are useful for recommending human calcium requirements to prevent osteoporosis.

107 2 A 2009

Project Number: 5450-51000-039-00D Accession: 0409965 FY: 2010

06 The calcium requirement for optimal bone health in the rat is similar whether based c bone mass, structure, or biomechanical strength criteria. Calcium supplementation increases bone density but the increase is small and the impact on bone strength and fracture risk is uncertain. ARS scientists at Grand Forks, ND investigated whether dietary calcium requirements differ for optimizing bone mass, structure, or biomechanical strength in rats. Bone mass, structure and strength all optimized with the same amount of dietary calcium (~2.5 grams of calcium per kilogram of diet), indicating that bone breaking strength and structural properties are not improved by increasing dietary calcium intakes beyond those needed to maximize bone density. Thes animal results can help in comprehending human calcium requirements, as human measurements are commonly limited to bone density.

107 2 A 2009

07 Pinto bean hull extract supplementation favorably affects markers of bone metabolism and bone structure in mice. Dry edible beans have many health benefits due to their high content of protein, non-digestible starches, fiber, and other bioactive components. Hulls from dry edible beans are rich in phenolic compounds recognized as possessing antioxidant activity. ARS scientists at Grand Forks, ND, showed that bean hull extract supplementation at 800 milligram/kilogram for 3 months decreased serum tartrate-resistant acid phosphatase and parathyroid hormone concentrations in mice. Bean hull extract supplementation also improved bone structural indices, bone mineral density and trabecular thickness in the third lumbar vertebra. These findings suggest that bean hull extract may have beneficial effects on bone health by decreasing bone resorption.

107 2 A 2009

08 New methodology developed for quantification of normal cell death in human white bloc cells. The ability of white blood cells to undergo controlled ell death is an essential feature in the maintenance and regulation of the immune response. ARS scientists at the Grand Forks Human Nutrition Research Center developed a method to assess the potential of white blood cells to undergo cell death in the intact whole blood sample. Whole blood collected from 30 free-living individuals was mixed with chemicals known to stimulate cell death. As cells begin to die, their DNA starts to break at characteristic points. Antibodies that target these broken ends were added and the blood sample was passed through an analyzer that counted each cell and the amount of attached antibody. This method appears capable of measuring the potential of white blood cells to go through a normal life cycle while minimizing unintentional physical damage to the cells during the assessment process.

107 2 A 2009

5. Significant Activities that Support Special Target Populations

None

Project Number: 5450-51000-039-00D Accession: 0409965 FY: 2010

6. Technology Transfer

0 Number of New CRADAs
0 Number of Active CRADAs
0 Number of New MTAs (providing only)
0 Number of Invention Disclosures Submitted
0 Number of Patent Applications Filed
0 Number of New Germplasm Releases
0 Number of new commercial licenses granted
0 Number of web sites managed
0 Number of non-peer reviewed presentations and proceedings
0 Number of newspaper articles and other presentations for non-science audiences
0 Number of Other Technology

7. International Cooperation / Collaboration

Scientific Publications: Log 115

1. Cao, J.J., Gregoire, B.R., Sheng, X., Liuzzi, J.P. 2010. Pinto Bean Hull Extract Supplementation Favorably Affects Markers of Bone Metabolism and Bone Structure in Mice. Food Research International. 43(2):560-566. 000023647

2. Cao, J.J., Sun, L., Gao, H. 2010. Diet-induced Obesity Alters Bone Remodeling Leading to Decreased Femoral Trabecular Bone Mass in Mice. Annals of the New York Academy of Sciences. 1192:292-297. 000024602

3. Nielsen, F.H. 2009. Dietary Fatty Acid Composition Alters Magnesium Metabolism, Distribution, and Marginal Deficiency Response in Rats. Magnesium Research. 22(4):280-288. 000024642

4. Nielsen, F.H. 2009. Micronutrients in Parenteral Nutrition: Boron, Silicon, and Fluoride. Gastroenterology. 137:S55-60. 000023436

5. Nielsen, F.H. 2010. Silicon Deprivation Does Not Significantly Modify the Acute White Blood Cell Response but Does Modify Tissue Mineral Distribution Response to an Endotoxin Challenge. Biological Trace Element Research. 135:45-55. 000024266

6. Nielsen, F.H. 2010. Magnesium, Inflammation, and Obesity in Chronic Disease. Nutrition Reviews. 68(6):333-340. doi:10.1111/j.1753-4887.2010.00293.x 000025060

7. Shen, C., Yeh, J.K., Cao, J.J., Wang, J. 2009. Green Tea and Bone Metabolism. Nutrition Research. 29(7):437-56. 000023741

Approved: MCGUIRE MICHAEL R Date: 09/27/2010

Project Number: 5450-51000-039-11T **Accession:** 0418308 **FY:** 2010

ModeCode: 5450-20-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER
DIETARY PREVENTION OF OBESITY-RELATED RESEARCH

NPL Leader: MARY J KRETSCH **Prin Invs:** GERALD F COMBS

Start Date: 10/01/2009 **Term Date:** 12/31/2009

National Programs: 107 N Human Nutrition

Title: FACTORS AFFECTING CELLULAR MINERAL UPTAKE

Period Covered **From:** 10 / 2009 **To:** 9 / 2010 **Final Report?** Yes
Terminate in Two Months? No

Agreement Number: 58-5450-0-0428

Organization Name: COLORADO STATE UNIVERSITY

Progress and Outcomes:

1a. **Objectives (from AD-416)**

Identify the metabolic roles of calcium and other ions affecting intracellular calcium uptake, with a focus on applications in in vitro fertilization.

1b. **Approach (from AD-416)**

Using equine in vitro fertilization models, determine effect of in vitro treatments designed to enhance the uptake of calcium by cultured cells including fertilized ova. The net effect of nutrient treatment on fertilization success will be evaluated.

3. **Progress Report**

This report documents research conducted under a Trust Agreement between ARS and COLORADO STATE UNIVERSITY. Additional details for the research can be found in the report for the parent project 5450-51000-039-00D, MINERAL INTAKES FOR OPTIMAL BONE DEVELOPMENT AND HEALTH

The project was completed. Analyses of samples conducted at the Grand Forks Human Nutrition Research Center were sent in a final report to collaborators at Colorado State University.

NP / Component Coding

Approved: MCGUIRE MICHAEL R **Date:** 10/04/2010

Project Number: 5450-51000-041-00D **Accession:** 0415292 **FY:** 2010

ModeCode: 5450-10-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER
HEALTHY BODY WEIGHT RESEARCH

NPL Leader: DAVID M KLURFELD **Prin Invs:** WILLIAM T JOHNSON

Start Date: 01/23/2009 **Term Date:** 05/23/2010

National Programs: 107 N Human Nutrition

Title: MITOCHONDRIAL FUNCTION AND NUTRITIONAL PROGRAMMING IN THE PREVENTION OF DIET-RELATED DISEASE

Period Covered **From:** 10 / 2009 **To:** 9 / 2010 **Final Report?** Yes
Terminate in Two Months? No

Progress and Outcomes:

1a. Objectives (from AD-416)

Overall, to determine, using animal models, whether iron (Fe), zinc (Zn), copper (Cu), or protein intakes optimize mitochondrial function either directly or through nutritional programming during early development to facilitate the prevention of diet-related diseases, with major emphasis on cardiovascular disease. Specific objectives are: (1) determine whether maternal protein restriction produces epigenetic changes in offspring that result in impaired mitochondrial function, vascular function or other metabolic or physiologic parameters; (2) determine whether placental insufficiency that causes global fetal undernutrition rather than maternal undernutrition leads to epigenetic changes that compromise physiological function in later life of the offspring; (3) determine if marginal intakes of Fe or Zn cause oxidative and nitrative damage to proteins, lipids and DNA in cardiac mitochondria by overproduction of reactive oxygen species caused by perturbations in the electron transport chain; (4) determine if marginal Fe or Zn intakes promote apoptosis in cardiomyocytes; (5) determine the relationship between marginal intakes of Fe, Cu or Zn during pregnancy and lactation and age-related cardiac pathology in the first generation caused by altered expression of genes encoding proteins of the electron transport chain in cardiac mitochondria; and (6) determine whether marginal Fe, Cu or Zn intakes lead to the development of hypertension through reactive oxygen mediated vascular injury.

1b. Approach (from AD-416)

Three approaches using laboratory animals will be used: (1) to determine the influence of maternal diets on nutritional programming during early development, female rats will be fed diets containing either marginal levels of the nutrient of interest (protein, Fe, Zn or Cu) or, as control animals, normal nutrient levels throughout pregnancy and lactation; (2) to determine the effects of placental insufficiency in rats, uteroplacental perfusion pressure will be reduced by surgically restricting the blood supply to the uterus on gestational day 14; and (3) to determine the effects of low Fe and Zn intakes on cardiac mitochondrial function, weanling rats will be fed diets containing marginally deficient levels of these minerals for 6-8 weeks. Offspring of rats subjected to maternal dietary restrictions or reduced uteroplacental perfusion pressure will be tested for epigenetic changes, cardiac mitochondrial dysfunction, cardiac oxidative damage, cardiomyocyte apoptosis and altered vascular responses at various ages ranging from 21 days to 1 year. Weanling rats subjected to direct dietary treatments will be similarly tested at the end of the diet treatment period. Epigenetic changes will be assessed by determining DNA methylation and the up- and/or down-regulation of

differentially methylated genes will be confirmed by real-time PCR. Measurements of mitochondrial function will include respiration, respiratory complex activity and composition, and reactive oxygen production. Mitochondria are a major source of reactive oxygen species and have a key role in regulating apoptosis. Assessment of the outcomes of mitochondrial dysfunction will extend to measurement of oxidative and nitrosative damage to mitochondrial proteins and DNA and of the susceptibility of cardiomyocytes to apoptosis. Blood pressure and vascular responses to constrictors and relaxants will be measured to determine the influences maternal treatments on vascular function in offspring and the direct effects of dietary treatments in weanling rats.

2. **Milestones for FY2010**

1. Establish telemetry protocol for assessing blood pressure, initiate maternal protein restriction animal study, collect tissue samples from first generation and begin analyses.
   Milestone Not Met
   Redirection (by Office of National Programs

2. Establish Western blotting protocols for 3-nitrotyrosine and 4-hydroxy-2-nonenal content in mitochondrial proteins.
   Milestone Substantially Met

3. Establish protocols for measuring mitochondrial membrane potential and difference spectra of cytochromes.
   Milestone Substantially Met

4. Establish protocol for the detection of 8-hydroxy-deoxyguanosine.
   Milestone Substantially Met

5. Initiate maternal iron feeding study to determine effect of low iron intake during pregnancy on cardiac mitochondrial function in offspring.
   Milestone Fully Met

3. **Progress Report**

The is the final report for Project 5450-51000-041-00D, which has been replaced by new OSQR-approved Project 5450-51000-047-00D that is being reported separately.

An experiment was completed that examined the effect marginal iron intake during pregnancy and lactation has on age-related function of cardiac mitochondria in the first generation. Female rats were placed on either low iron diet (15 mg Fe/g diet) or normal iron diet (35 mg Fe/g) for three weeks prior to conception and remained on the diet throughout pregnancy and lactation. Cardiac mitochondrial function in the offspring was assessed on postnatal days 1, 14 and 21. Cardiac mitochondrial function and body composition was also assessed in adult offspring following treatment with Fe adequate diet for six weeks starting on postnatal day 21. The data for mitochondrial function in the offspring were highly variable and inconclusive. Failure of the low iron diet to produce anemia in the dams may have led to the variability in the data obtained from the offspring. However, after consuming adequate iron for six weeks after weaning, it was a tendency for female offspring of dams fed low iron diet to have higher body weight and lower lean mass than female offspring of dams fed adequate iron. This suggests that the consumption of low iron during pregnancy and lactation may have long term effects on body composition in female offspring. However, the findings of this experiment indicate that dietary iron needs to be reduced to a level lower than 15 mg Fe/g during pregnancy and lactation to produce significant outcomes in cardiac

Project Number: 5450-51000-041-00D Accession: 0415292 FY: 2010

mitochondrial function in offspring.

NP / Component Coding

107 4 B 2009

4. Accomplishments

5. Significant Activities that Support Special Target Populations

None

6. Technology Transfer

0 Number of New CRADAs
0 Number of Active CRADAs
0 Number of New MTAs (providing only)
1 Number of Invention Disclosures Submitted
0 Number of Patent Applications Filed
0 Number of New Germplasm Releases
0 Number of new commercial licenses granted
0 Number of web sites managed
0 Number of non-peer reviewed presentations and proceedings
0 Number of newspaper articles and other presentations for non-science audiences
0 Number of Other Technology

Invention Disclosure Submitted Details:

01 Docket No: 210

Title: GENE METHYLATION AS BIOMARKERS OF PREECLAMPSIA

Descripton: Description: Develop a panel of genes that could be used to either indicate a predisposition to preeclampsia or to confirm the diagnosis of preeclampsia.
Transfer:Invention disclosure that will hopefully lead to a patent and commercialization of a gene panel for diagnosis of preeclampsia by a medical clinic or hospital.
Customer/User: The primary customer is a physician or clinical laboratory. The secondary customer is the woman for whom the panel is used.
Impact/Outcome: Preeclampsia, which can be passed on to offspring, affects up to 8% of women in the United States. Preeclampsia can result in placental insufficiency which in turn results in fetal growth restriction and predisposing the fetus to the development of adult disease. Currently preeclampsia is diagnosed by blood pressure elevation and proteinuria in the second half of pregnancy. Developing a panel of genes that could either indicate a predisposition to preeclampsia or to confirm the diagnosis of preeclampsia would be useful to confirm diagnosis or for screening women who are thinking of becoming pregnant and have mothers who had preeclampsia. Further, identification of the genes associated with preeclampsia would provide therapeutic targets for improved pregnancy outcome in both the mother and her infant.

Project Number: 5450-51000-041-00D **Accession:** 0415292 **FY:** 2010

7. International Cooperation / Collaboration

Scientific Publications: Log 115

1. Anderson, C.M., Johnson, W.T. 2010. Maternal Copper Deficiency Perpetuates Altered Vascular Function in Sprague-Dawley Rat Offspring. Journal of Developmental Origins of Health and Disease. 1(2):131-140. 000023288
2. Schuschke, D.A., Adeagbo, A.S., Patibandla, P.K., Fernandez-Botran, R., Johnson, W.T. 2009. Cyclooxygenase-2 is Upregulated in Copper-Deficient Rats. Inflammation. 32(5):333-339. 000024029

Approved: MCGUIRE MICHAEL R **Date:** 09/29/2010

Project Number: 5450-51000-042-00D **Accession:** 0415303 **FY:** 2010

ModeCode: 5450-20-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER
DIETARY PREVENTION OF OBESITY-RELATED RESEARCH

NPL Leader: JOHN W FINLEY **Prin Invs:** LIN YAN

Start Date: 01/15/2009 **Term Date:** 05/26/2010

National Programs: 107 N Human Nutrition

Title: MINERAL UTILIZATION AND BIOAVAILABILITY IN THE 21ST CENTURY, WITH CHANGING DIETS AND AGRICULTURAL PRACTICES

Period Covered From: 10/2009 **To:** 9 /2010 **Final Report?** Yes
Terminate in Two Months? No

Progress and Outcomes:

1a. Objectives (from AD-416)

The general objective is to determine how current and proposed changes to the American diet that may adversely affect intake and/or how bioavailability of the essential mineral nutrients can be modified to enhance trace element nutrition, with emphasis on selenium (Se), iron (Fe), zinc (Zn), and copper (Cu). Specific objectives are:

Objective 1: Determine how shifts in agricultural and dietary practices, such as the availability of functional/genetically modified foods and emphasis on plant-based diets with reductions in meat consumption will impact the intake, bioavailability, and dietary requirements of minerals. This objective will address the production of foods with enhanced bioactive Se compounds, and assess their ability to enhance health, especially by controlling oxidative stress and reducing cancer risk. The impact of organic farming methods will also be assessed (Finley). It will also address the practical impact of dietary changes that emphasize plant-based diets on meeting nutritional needs for Fe and Zn (Hunt).

Objective 2: Determine the effectiveness of current and proposed mineral fortification/supplementation practices for improving mineral nutrition while avoiding excessive or imbalanced mineral intakes. This objective will evaluate the bioavailability of Fe fortificants such as elemental Fe and micronized, encapsulated Fe compounds in human studies (Hunt).

Objective 3: Determine the mechanisms of uptake, transport, and retention of food minerals and how mineral nutritional status influences these mechanisms to impact the bioavailability of essential minerals, non-nutritive metals, and other food components. Cell and whole animal models will be employed to elucidate how the modifications of mineral content of foods can influence the biochemical regulation of specific transporters, cellular trafficking, and interactions of minerals such as Zn, Fe, Cu, Cd, Se, and Mn. (Reeves).

Problem to be addressed with increased funds: Elucidate the roles and diets in support of optimal health and prevention of obesity and related illnesses, cardiovascular disease, osteoporosis and cancer.

Problem to be addressed with increased funds (FY05): Under Performance Measure 4.1.1 of the ARS Strategic Plan and the NP107 Action Plan, this project will develop an enhancement to the food supply by increasing the nutritional value of beef.

Project Number: 5450-51000-042-00D Accession: 0415303 FY: 2010

Objective modification FY05: Increase the amount of omega-3 fatty acids in beef to a nutritionally significant level by feeding flax. Demonstrate that the increase in omega-3 fatty acids in the meat are sufficient to have a physiological effect. Study feasibility of increasing selenium in beef to levels that will have an impact on human health when the meat is consumed at recommended levels. This may include studies of organic form of selenium in beef, stability with varying cooking methods, sensory issues, bioavailability and health effects in both steers and consumers.

1b. Approach (from AD-416)

Methodology will include tests of agricultural conditions affecting the amounts and forms of minerals incorporated into in foods; in vitro, cellular, and animal models of mineral transport and absorption; and human experiments with controlled diets to assess mineral absorption, retention, and biological function and to model nutritional requirements.

Specific objectives to be accomplished with increased funding: To study the roles of foods, particularly those produced in the Northern Plains, in the support of health. This work is to be multi-disciplinary, including collaborations such as with the University of North Dakota School of Medicine and Health Sciences and North Dakota State University.

2. Milestones for FY2010

1. Assess bioavailability of Se from soybeans, peas and oats produced in selenium rich Northern Plains.

   Milestone Fully Met

3. Progress Report

The is the final report for bridging project 5450-51000-042-00D, which has been replaced by new OSQR-approved Project 5450-51000-048-00D that is being reported separately.

During the course of this project, we completed experiments and analyses that assessed bioavailability of selenium from high-selenium soybeans, peas and oats produced in South Dakota. Any work left for this project involves completion of manuscripts. This CRIS project will not be continued because of the Center's re-direction to obesity-related research.

NP / Component Coding

107 1 C 2009

4. Accomplishments

01 Selenium from high-selenium crops from Northern Plains is bioavailable. Selenium is a essential nutrient to humans, and agricultural produces from Northern Plains are high in this nutrient. ARS scientists in Grand Forks, North Dakota, completed feeding experiments and analyses that assessed selenium bioavailability from high-selenium soybeans, peas and oats produced in South Dakota, and found that selenium from these products was highly bioavailable to selenium-deficient rats compared with selenomethionine, a food form of selenium. These results may lead to further studies assessing the nutritional values and health benefits of this natural dietary source c selenium, and these results will increase the marketability of agricultural products

Project Number: 5450-51000-042-00D Accession: 0415303 FY: 2010

from Northern Plains.

107 1 C 2009

5. Significant Activities that Support Special Target Populations

6. Technology Transfer

0 Number of New CRADAs
0 Number of Active CRADAs
0 Number of New MTAs (providing only)
0 Number of Invention Disclosures Submitted
0 Number of Patent Applications Filed
0 Number of New Germplasm Releases
0 Number of new commercial licenses granted
0 Number of web sites managed
0 Number of non-peer reviewed presentations and proceedings
0 Number of newspaper articles and other presentations for non-science audiences
0 Number of Other Technology

7. International Cooperation / Collaboration

Scientific Publications: Log 115

1. Beisiegel, J.M., Klevay, L.M., Johnson, L.K., Hunt, J.R. 2009. Zinc Absorption Adapts to Zinc Supplementation in Postmenopausal Women. Journal of the American College of Nutrition. 28(2):177-183. 000019441

2. Hadley, K.B., Newman Jr, S.M., Hunt, J.R. 2010. Dietary Zinc Reduces Osteoclast Resorption Activities and Increases Markers of Osteoblast Differentiation, Matrix Maturation, and Mineralization in the Long Bones of Growing Rats. Journal of Nutritional Biochemistry. 21(4):297-303. 000022036

3. Long, E.K., Rosenberger, T.A., Picklo, M.J. 2010. Ethanol Withdrawal Increases Glutathione Adducts of 4-Hydroxy-2-Hexenal but not 4-Hydroxyl-2-Nonenal in the Rat Cerebral Cortex. Free Radical Biology and Medicine. 48(3):384-390. 000024479

Approved: MCGUIRE MICHAEL R Date: 09/28/2010

Project Number: 5450-51000-044-00D **Accession:** 0415317 **FY:** 2010

ModeCode: 5450-20-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER
DIETARY PREVENTION OF OBESITY-RELATED RESEARCH

NPL Leader: DAVID M KLURFELD **Prin Invs:** ERIC O UTHUS

Start Date: 01/26/2009 **Term Date:** 03/16/2010

National Programs: 107 N Human Nutrition

Title: ROLE OF DIETARY SELENIUM ON GENE EXPRESSION, CELL CYCLE AND MOLECULAR MECHANISMS IN CANCER RISK

Period Covered From: 10/2009 **To:** 9 /2010 **Final Report?** Yes
Terminate in Two Months? No

Progress and Outcomes:

1a. Objectives (from AD-416)

Determine the molecular and cellular mechanism(s) of action of selenium (Se) in anti-carcinogenesis. Specific objectives include 1) Determine the role of Se in cell cycle progression and apoptosis in models of colon cancer; 2) Determine the role of selenoproteins in cancer prevention and the role of dietary components in the regulation of selenoprotein activity; 3) Determine the mechanism(s) by which Se alters DNA methylation and 4) Determine the relationship of oral selenium intake with selenium status and indicators of cancer risk.

1b. Approach (from AD-416)

A variety of cell culture and animal model approaches will be used. In general, cell culture experiments will be run using cell lines specific for colon. Various forms and concentrations of selenium will be added to serum-free media. Cell growth, indices of selenium status, and indices of cell cycle progression and apoptosis will be measured. These studies will be used to determine the effects of nutritional levels of selenium in supporting cellular survival signaling in human cultured colon cells, and the role of the putative anti-tumorigenic selenium-metabolite, methylselenol, in cell cycle progression and apoptosis in human cultured colon cells. Other cell culture models (colon and/or liver cell lines) will be used in siRNA knockdown studies. These experiments will determine the effect of selenium in cells in which specific genes have been knocked down by siRNA. Other studies will use knock downs of various selenoproteins to determine their role in anticarcinogenicity of selenium. Animal studies will use rats and mice to determine the effects of form and concentration of dietary selenium on 1) selenoprotein expression and activity as related to carcinogenesis, 2) carcinogen-induced aberrant crypt formation (preneoplastic colon cells) and, 3) indices of oxidative stress and one-carbon metabolism including DNA methylation of genomic and gene specific DNA.

2. Milestones for FY2010

1. Complete animal feeding, data collection and analysis (tumor numbers, size and related measures and Se analysis for an experiment that compares Se compounds on secondary cancer prevention.
   Milestone Fully Met

2. Establish cell models for an experiment to test the hypothesis that CH3SeH induces the expression of the APC/Wnt/b-catenin and K Ras pathways.
   Milestone Fully Met

Project Number: 5450-51000-044-00D **Accession:** 0415317 **FY:** 2010

3. Develop protocol (Identify effects of dietary Se on markers of oxidative DNA damage biomarkers related to cancer risk in humans), gain IRB approval, initiate recruiting.
Milestone Substantially Met

4. Develop protocol (Determine whether consumption of SeMet affects expression of genes related to cancer risk), gain IRB approval, initiate recruiting.
Milestone Fully Met

5. Develop analytical method (Characterize the non-protein-bound Se in plasma and determine its relationship with other biomarkers of Se status).
Milestone Substantially Met

6. Develop protocol (Determine whether Se metabolism varies according to GPX1 genotype), gain IRB approval; begin recruiting and subject screening.
Milestone Fully Met

7. Develop protocol (Determine whether single-carbon metabolic status is related to BMI and/or plasma Se response to increased SeMet consumption), gain IRB approval; identify subjects from GFHNRC #HS009 trial for these analyses.
Milestone Fully Met

3. **Progress Report**

The is the final report for bridging Project 5450-51000-044-00D, which has been replaced by new OSQR-approved Project 5450-51000-045-00D that is being reported separately.

A number of studies were designed and undertaken to determine the mechanism(s) of chemoprevention by the nutrient selenium - major accomplishments from those studies are listed below. Any work left for this project involves completion of manuscripts.

The project covered by this reporting period is a continuation of Project No: 5450-51000-036-00D and a new 5-year plan entitled "Mechanisms of Cancer Prevention by Selenium". Because of program redirection the plan "Mechanisms of Cancer Prevention by Selenium" was not approved but used to redirect our research to the newly approved CRIS project entitled "Dietary Modulation of Obesity-Related Cancer by Selenium". Because the new project focuses on obesity-related cancer, our work has centered around that. For example, we have continued the development of animal models that can be used to show that dietary obesity enhances secondary tumor development and tumor growth. Development of these animal models will be crucial for studies on dietary intervention and prevention of obesity-related secondary cancer. A typical part of the Western diet is a high fat intake that leads to increased levels of fecal bile acids (primarily, deoxycholic acid), which are believed to promote colon carcinogenesis. It is also known that colon tumor development is driven by the accumulation of dysregulation in cellular MAPK/APC cellular signaling and altered epigenetic status (e.g., p53 gene and global DNA methylation). Cell models that we have developed will be used to determine whether methylselenol antagonizes the effect on cellular MAPK/APC signaling and epigenetic status caused by deoxycholic acid. We also developed a voluntary physical activity model for the mouse. This model will be useful in investigations of physical activity and/or its combination with dietary modifications on obesity-related cancer development and growth.

NP / Component Coding

107 2 A 2009

Project Number: 5450-51000-044-00D **Accession:** 0415317 **FY:** 2010

107 3 A 2009

4. Accomplishments

01 Methylselenol, a selenium metabolite, inhibits tumor cell growth and invasion. Methylselenol has been hypothesized to be a critical selenium metabolite for anticancer activity in vivo, and our previous studies demonstrated that very small amounts of methylselenol inhibits the migration and invasive potential of tumor cells in a cell culture model. However, little is known about the association between cance signal pathways and methylselenol's inhibition of tumor cell invasion. ARS scientists in Grand Forks, North Dakota, demonstrated that methylselenol exposure inhibited cell growth. They also used a cancer signal pathway-specific array containing 15 different signal transduction pathways involved in oncogenesis to study the effect of methylselenol on cellular signaling. Taken together, these studies identify 7 novel methylselenol responsive genes and demonstrate that methylselenol inhibits specific cancer signaling pathways which may contribute to the inhibition of tumor cell invasion.

107 2 A 2009

02 Selenium inhibits metastasis in certain cancer mouse models. Selenium is an essentia nutrient, and its cancer-preventive potential has been studied in both humans and laboratory animals. Investigations conducted by ARS scientists in Grand Forks, North Dakota, focused on selenium and secondary cancer prevention. Our preliminary result showed that a methylated metabolite of selenium, methylseleninic acid, had an inhibitory effect on secondary tumor formation in one of two models studied for cance metastasis. Data from these experiments are useful in experimental design for futur investigation on selenium and secondary cancer prevention.

107 2 A 2009

5. Significant Activities that Support Special Target Populations

We found that women regulate selenium metabolism somewhat differently than men. When consuming comparable amounts of dietary selenomethionine, women retain less than men, which we believe may reflect an increased turnover rate compared to men.

6. Technology Transfer

0 Number of New CRADAs
0 Number of Active CRADAs
0 Number of New MTAs (providing only)
0 Number of Invention Disclosures Submitted
0 Number of Patent Applications Filed
0 Number of New Germplasm Releases
0 Number of new commercial licenses granted
0 Number of web sites managed
0 Number of non-peer reviewed presentations and proceedings
0 Number of newspaper articles and other presentations for non-science audiences
0 Number of Other Technology

7. International Cooperation / Collaboration

Scientific Publications: Log 115

Project Number: 5450-51000-044-00D **Accession:** 0415317 **FY:** 2010

1. Chiang, E.C., Shen, S., Kengeri, S.S., Xu, H., Combs, G.F., Morris, J.S., Bostwick, D.G., Waters, D.J. 2010. Defining the Optimal Selenium Dose for Prostate Cancer Risk Reduction: Insights from the U-Shaped Relationship Between Selenium Status, DNA Damage, and Apoptosis. Dose Response. 8:285-300. **000024322**

2. Yan, L., Graef, G.L., Reeves, P.G., Johnson, L.K. 2009. Selenium Bioavailability from Soy Protein Isolate and Tofu in Rats Fed a Torula Yeast-Based Diet. Journal of Agriculture and Food Chemistry. 57:11575-11580. **000023889**

3. Yan, L., Spitznaagel, E.L., Bosland, M.C. 2010. Soy Consumption and Colorectal Cancer Risk in Humans: A Meta-Analysis. Cancer Epidemiology Biomarkers and Prevention. 19(1):148-158. **000024457**

4. Zeng, H., Botnen, J.H., Briske Anderson, M.J. 2010. Deoxycholic Acid and Selenium Metabolite Methylselenol Exert Common and Distinct Effects on Cell Cycle, Apoptosis, and MAP Kinase Pathway in HCT116 Human Colon Cancer Cells. Nutrition and Cancer. 62(1):85-92. **000023158**

5. Zeng, H., Wu, M., Botnen, J.H. 2009. Methylselenol, a Selenium Metabolite, Induces Cell Cycle Arrest in G1 Phase and Apoptosis via the Extracellular-Regulated Kinase 1/2 Pathway and Other Cancer Signaling Genes. Journal of Nutrition. 139:1613-1618. **000023790**

Approved: MCGUIRE MICHAEL R **Date:** 09/28/2010

Project Number: 5450-51530-010-01R **Accession:** 0412541 **FY:** 2010

ModeCode: 5450-10-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER
HEALTHY BODY WEIGHT RESEARCH

NPL Leader: JOHN W FINLEY **Prin Invs:** HENRY C LUKASKI

Start Date: 10/01/2007 **Term Date:** 12/31/2009

National Programs: 107 N Human Nutrition

Title: EFFICACY OF ZINC SUPPLEMENTATION ON DIARRHEA INCIDENCE IN AN ADULT POPULATION IN WESTERN KENYA

Period Covered **From:** 10/2009 **To:** 9 /2010 **Final Report?** Yes
Terminate in Two Months? No

Agreement Number: 60-5450-8-0400

Organization Name: U.S. ARMY RESEARCH INSTITUTE OF ENVIRONMENTAL MEDICINE

Progress and Outcomes:

1a. **Objectives (from AD-416)**

ARS will receive blood samples and measure blood biochemical indicators of iron, zinc, selenium nutritional status and indicators of inflammation of human volunteers.
ARS will ship samples for vitamin A and retinol-binding protein to Pennington Research Center where USARIEM has a contract to run their blood chemistries.
ARS will provide the results of analytical tests to US Army Research Institute of Environmental Medicine (USARIEM) co-investigators.
USARIEM will recruit human volunteers, randomize volunteers to treatment groups, and provide supplements and placebo treatments.
USARIEM will obtain, prepare and ship blood samples to ARS.
USARIEM will recruit and train field research associates who will collect data on diarrhea incidence and symptoms.
USARIEM collaborators will evaluate the effects of zinc supplementation on clinical assessments of diarrhea and some potential mediating factors.
ARS and USARIEM jointly will participate in interpretation of findings and preparation of reports and manuscripts.

1b. **Approach (from AD-416)**

The study will use a double-blind (observer blind and volunteer blind), randomized controlled design (randomization ratio 1:1) of supplemental zinc (20 mg/d) compared to placebo (maltodextrin) for five months. Randomization will include a total of 500 eligible adults matched by sex and age (18 to 55 years) and living in Western Kenya. This field research will be supervised and coordinated by investigators of the US Army Medical Research Unit - Kenya (USAMRU-K) and the Kenya Medical Research Institute (KEMRI)/Walter Reed Project (WRP), and conducted at the Kombewa Clinical Research Center (KCRC) outside of Kisumu in Western Kenya. This study will test the hypothesis that zinc supplementation reduces the incidence and symptoms of diarrhea and decreases presence of bacterial vectors associated with diarrhea.

3. **Progress Report**

This report documents research conducted under a Reimbursable Agreement between ARS and the U.S. ARMY RESEARCH INSTITUTE OF ENVIRONMENTAL MEDICINE (USARIEM). Additional details for the research can be found in the report for the parent project 5450-51530-010-00D, MICRONUTRIENT ROLES IN PHYSIOLOGY AND HEALTH

Project Number: 5450-51530-010-01R **Accession:** 0412541 **FY:** 2010

The project constituted collaborative studies of the Grand Forks Human Nutrition Research Center and the USARIEM to determine the efficacy of zinc supplementation in the prevention of chronic diarrhea in an area where that problem is endemic. We completed the supplementation trial and analysis of blood samples for biomarkers of inflammation (C-reactive protein), iron status (serum ferritin), and other trace elements and electrolytes. We found that supplemental zinc reduced the incidence of diarrhea in Kenyan adults. A final report of all analytical data was sent to collaborators at USARIEM.

NP / Component Coding

Approved: MCGUIRE MICHAEL R **Date:** 10/05/2010

Project Number: 5450-51530-010-03N **Accession:** 0411613 **FY:** 2010

ModeCode: 5450-10-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER
HEALTHY BODY WEIGHT RESEARCH

NPL Leader: MARY J KRETSCH **Prin Invs:** HENRY C LUKASKI

Start Date: 02/01/2007 **Term Date:** 12/31/2009

National Programs: 107 N Human Nutrition

Title: DIET AND EXERCISE ON PROTEIN EXPRESSION IN MUSCLE

Period Covered **From:** 10/2009 **To:** 9 /2010 **Final Report?** Yes
Terminate in Two Months? No

Agreement Number: 58-5450-7-0110N

Organization Name: US ARMY RES INST ENVIR MEDICINE

Progress and Outcomes:

1a. **Objectives (from AD-416)**

To identify micro-nutrient responsive proteins in muscle and other tissues obtained from rodent models.

1b. **Approach (from AD-416)**

Laboratory rodents of varying ages and, in some cases varying genotypes and phenotypes, will be fed diets containing micronutrients in marginally-deficient and adequate amounts and either exposed to physical training or untrained. Comparisons will be made among established biochemical and physical markers of nutritional status and expression of proteins in selected tissues to determine impacts of sub-clinical micronutrient deficiencies. Emphasis will be muscle mitochondrial complexes and signal transduction in mitogenesis and angiogenesis.

3. **Progress Report**

This report documents research conducted under a Non Funded Cooperative Agreement between ARS and the U.S. ARMY RESEARCH INSTITUTE OF ENVIRONMENTAL MEDICINE (USARIEM). Additional details for the research can be found in the report for the parent project 5450-51530-010-00D, MICRONUTRIENT ROLES IN PHYSIOLOGY AND HEALTH

The project constituted collaborative studies of the Grand Forks Human Nutrition Research Center and the USARIEM in the broad area of interaction of diet and physical activity on expression of proteins that regulate structural and functional adaptations of skeletal muscle and other key organs. We completed analyses of samples collected in a study to determine the effect of exercise (swimming) duration on the use of fat/carbohydrate for energy production by muscle in the rat model. Our findings showed that prolonged exercise increased this control, but that this was not achieved by exercise-induced food (energy) restriction. A final report of all results was sent to the collaborator at USARIEM.
ADODR monitoring included phone calls, e-mails, and meetings.

NP / Component Coding

Approved: MCGUIRE MICHAEL R **Date:** 09/23/2010

Project Number: 5450-51530-010-04T **Accession:** 0412129 **FY:** 2010

ModeCode: 5450-10-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER
HEALTHY BODY WEIGHT RESEARCH

NPL Leader: JOHN W FINLEY **Prin Invs:** FORREST H NIELSEN

Start Date: 05/01/2007 **Term Date:** 12/31/2009

National Programs: 107 N Human Nutrition

Title: MAGNESIUM NUTRITION AND SLEEP BEHAVIOR IN OLDER ADULTS

Period Covered **From:** 10/2009 **To:** 9 /2010 **Final Report?** Yes
Terminate in Two Months? No

Agreement Number: 58-5450-7-0431

Organization Name: TYRASE RESEARCH

Progress and Outcomes:

1a. **Objectives (from AD-416)**

The objective of this cooperative research project is to determine the association between magnesium nutrition (intakes and status) and sleep behavior (quantity, quality, disturbances) in older adults; to determine the efficacy of magnesium supplementation to improve sleep (increase quantity and quality and prevent or reduce disorders); and to identify factors (for example, gender, health, diet, body composition, physical activity, depression - historical or current) that mediate or moderate the relationship between magnesium nutrition and sleep.

1b. **Approach (from AD-416)**

An experiment will be performed that will have an 8-week double-blind placebo-controlled cross-sectional design. People with sleep complaints (for example, insomnia, nighttime awakenings, difficulty in falling asleep, awakening too early, not feeling rested after sleep) will be recruited. Following baseline assessment during week one of past and current health, diet, body composition, physical activity, depression, and sleep, 100 adults (50 males and 50 females) aged older than 51 yrs will be randomly assigned to one of two groups of 50 each. Groups will be matched by gender, age and overall sleep score and magnesium status (determined by erythrocyte magnesium and calcium, and plasma total and ionized magnesium). Then one group will be given a 300 mg/day magnesium gluconate supplement for 7 weeks while the other group will be given a placebo. An assessment of health, diet, body composition, physical activity, depression, sleep and magnesium status will occur during weeks 6 and 8, concluding the study.

3. **Progress Report**

This report documents research conducted under a Trust Agreement between ARS and TYRASE RESEARCH. Additional details for the research can be found in the report for the parent project 5450-51530-010-00D, MICRONUTRIENT ROLES IN PHYSIOLOGY AND HEALTH

The purpose of the research was to determine whether a low magnesium status contributes to the high prevalence of sleep disturbances in older adults. Sleep quality as determined by the overall Pittsburg Sleep Quality Index was significantly improved regardless of whether the subjects received the magnesium supplement or placebo. Red blood cell magnesium also increased regardless of supplementation. The reason for the overall increase is unclear, but may be related to increased citrate intake with meals.

Project Number: 5450-51530-010-04T Accession: 0412129 FY: 2010

Magnesium was supplemented as magnesium citrate and the placebo was sodium citrate. When all subjects were included in the analyses, magnesium supplementation did not significantly affect numerous biochemical variables that respond to a severe magnesium deficiency in experimental animals. However, when sub-groups were examined, magnesium supplementation significantly reduced C-reactive protein (CRP) in subjects whose baseline values were higher than 3.0 (an indication of inflammatory stress). Thirty-seven subjects had baseline serum magnesium concentrations below 1.8 mg/mL, the low value for normal serum magnesium. When only these subjects were included in the analysis, both serum magnesium and calcium significantly increased during the study with the increase more marked in the magnesium-supplemented group. Food diary data showed that 44 of the 78 women and 14 of the 22 men, or 58% of the subjects that started the study were consuming less than the Estimated Average Requirement (EAR) for magnesium set by the Food and Nutrition Board of the Institute of Medicine. The low magnesium intake was associated with higher CRP values. The findings indicate that a significant number of individuals older than 51 years have a low magnesium status, and that magnesium supplementation may alleviate some chronic low-grade inflammation, which has been associated with poor sleep deprivation, cardiovascular disease, and osteoporosis. A manuscript is being prepared reporting the findings that will be submitted to a journal publishing peer-reviewed articles.

Because the study was performed in-house, the ADODR actively participated in the research by conducting information meetings, assessing the validity of the procedures followed, and addressing problems with equipment, forms and procedures occurring during the study. Progress in this project was communicated by the ADODR through telephone calls and a final written report was sent to Tyrase Research.

NP / Component Coding

Approved: MCGUIRE MICHAEL R **Date:** 10/04/2010

Project Number: 5450-51530-010-07N **Accession:** 0410137 **FY:** 2010

ModeCode: 5450-10-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER
HEALTHY BODY WEIGHT RESEARCH

NPL Leader: MARY J KRETSCH **Prin Invs:** GERALD F COMBS

Start Date: 03/09/2006 **Term Date:** 09/30/2010

National Programs: 107 N Human Nutrition

Title: MINERAL NUTRITION RESEARCH

Period Covered **From:** 10 / 2009 **To:** 9 / 2010 **Final Report?** Yes
Terminate in Two Months? No

Agreement Number: 58-5450-6-0101N

Organization Name: US ARMY RES INST ENVIR MEDICINE

Progress and Outcomes:

1a. **Objectives (from AD-416)**

Collaborator in planning, implementation and reporting of research on the effects of minerals on human nutritional needs and physical and psychological performance.

1b. **Approach (from AD-416)**

Human volunteers will be studied under a variety of dietary conditions and biochemical and functional parameters will be measured.

3. **Progress Report**

This report documents research conducted under a Non Funded Cooperative Agreement between ARS and the U.S. ARMY RESEARCH INSTITUTE OF ENVIRONMENTAL MEDICINE (USARIEM). Additional details for the research can be found in the report for the parent project 5450-51530-010-00D, MICRONUTRIENT ROLES IN PHYSIOLOGY AND HEALTH

The project constituted collaborative studies of the Grand Forks Human Nutrition Research Center and the USARIEM in the broad area of nutrition research with emphasis on weight management and bone health. We developed a plan for a collaborative study to determine whether high-protein diets can be effective in mitigating the decline in resting energy expenditure and the losses of lean body mass and bone mineral density typically attending weight reduction caused by energy imbalance. The protocol for this collaborative study was developed and review by the respective institutional review boards of USARIEM and the University of North Dakota (for the GFHNRC). This study will be conducted at the GFHNRC starting in FY2011 under a new agreement with USARIEM.

ADODR monitoring is via phone calls and e-mails.

NP / Component Coding

Approved: MCGUIRE MICHAEL R **Date:** 10/04/2010